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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/748,853	12/30/2003	Carl J. Wheeler	1530.0260002	6433

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EXAMINER	
ROYDS, LESLIE A	
ART UNIT	PAPER NUMBER
1614	

MAIL DATE	DELIVERY MODE
08/06/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/748,853	WHEELER, CARL J.	
	Examiner	Art Unit	
	Leslie A. Royds	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *18 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *64-90* is/are pending in the application.

4a) Of the above claim(s) *65,66,75-82 and 88-90* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *64,67-74 and 83-87* is/are rejected.

7)☒ Claim(s) *74* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *18 March 2008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 64-90 are presented for examination.

Applicant's response filed April 4, 2007 to the previous Office Action dated February 23, 2007 has been received and entered into the present application. Pursuant to the notice dated September 20, 2007, Applicant's response was non-compliant. Applicant's response filed March 18, 2008 correcting the deficiencies stated in the notice dated September 20, 2007 was also received and entered into the present application.

Applicant's Information Disclosure Statement (IDS) filed March 18, 2008 has been received and entered into the present application. As reflected by the attached, completed copy of form PTO/SB/08a (two pages total), the Examiner has considered the cited references.

Claims 64-90 remain pending.

Rejections not reiterated from previous Office Actions are hereby withdrawn. The following rejections and objections are either reiterated or newly applied. They constitute the complete set of rejections and objections presently being applied to the instant application.

Requirement for Restriction/Election

Applicant's election **with traverse** of the invention of Group I (claims 64-70 and 83-86), directed to a method of delivering an anionic molecule into a cell, and the election of the species of DMRIE carboyxlate propyl amide as the single disclosed species of compound of the formula presented in claim 64, in the replies filed April 4, 2007 and March 18, 2008, is acknowledged by the Examiner.

Applicant traverses the requirement on the grounds that the invention of Group II, especially claims 71-74 and 87 also read on the elected species and, thus, the groups should be examined together.

Applicant's traversal has been fully and carefully considered.

In view of the fact that the invention of Group II is directed to the same purpose of delivering an

anionic molecule into a cell using a smaller subset of compounds of those recited in instant claim 64 (and also includes the single disclosed species of DMRIE carboxylate propyl amide), it appears that rejoinder of the invention of Group II with that of Group I is appropriate at this time. Accordingly, instant claims 64-74 and 83-88 will be under examination insofar as they read upon the elected species of DMRIE carboxylate propyl amide.

However, the restriction between claims 64-74 and 83-88 and the inventions of Group III (claims 75-78 and 89-90) and Group IV (claims 79-82) remains proper for the reasons already of record and further in view of the fact that Applicant has failed to advance any additional reasons or evidence in support of the lack of patentable distinction between the groups. Accordingly, the restriction remains proper.

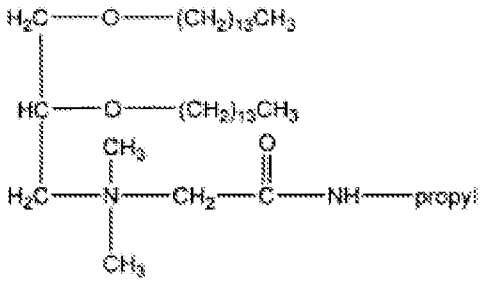
Therefore, for the reasons above and those made of record at pages 2-12 of the previous Office Action dated February 23, 2007, the requirement remains proper and is hereby made **FINAL**.

Claims 65-66, 75-82 and 88-90 are **withdrawn** pursuant to 37 C.F.R. 1.142(b) as being drawn to non-elected subject matter.

The claims corresponding to the elected subject matter are claims 64, 67-74 and 83-87 and such claims are herein acted on the merits.

Expansion of Election of Species Requirement

Search and examination of the instant claims was performed insofar as the instant claims read upon the elected species of DMRIE carboxylate propyl amide with the chemical structure of



as set forth in the reply filed March 18, 2008. A reasonable and comprehensive search determined that the prior art at the time of the invention was such that it did not anticipate or render obvious the elected specie of DMRIE carboxylate propyl amide for use in a method of delivering an anionic molecule into a cell. Accordingly, search and examination of the instant claims has been expanded to cover compounds of the formula presented in instant claim 64, wherein:

(1) R1 and R2 are linear or branched, unsubstituted or substituted C1-C23 alkyl;

(2) R3 and R4 are hydrogen or linear or branched, unsubstituted or substituted C1-C23 alkyl;

(3) Z is oxygen;

(4) R6 is hydrogen or equivalent to R1, R2, R3 or R4 (i.e., in this case, R6 may also be linear or branched, unsubstituted or substituted C1-C23 alkyl);

(5) n is 1-6 and m is 1-10;

(6) Y is a pharmaceutically acceptable anion.

Objection to the Claims (New Grounds of Objection)

Claim 74 is objected to for reciting a “compound according to claim 73", where claim 73 is directed to a method. Appropriate correction is required. For the purposes of examination, claim 74 will be interpreted as a "method according to claim 73”.

Claim Rejections - 35 USC § 112, Second Paragraph (New Grounds of Rejection)

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 64, 67-74 and 83-87 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention.

Present claim 64 is directed to a method of delivering an anionic molecule into a cell comprising (a) contacting the anionic molecule with a composition comprising an effective amount of a compound according to the formula presented in the claim, and (b) contacting a cell with the lipid complex formed in step (a) whereby a biologically effective amount of the anionic molecule is delivered into the cell.

Present claim 71 is directed to a method of delivering an anionic molecule into a cell comprising (a) contacting the anionic molecule with a composition comprising an effective amount of a compound according to the formula presented in the claim, and (b) contacting a cell with the lipid complex formed in step (a), whereby a biologically effective amount of the anionic molecule is delivered into the cell.

Regarding instant claim 64 or 71, there is insufficient antecedent basis for the limitation "the lipid complex" in each of claims 64 and 71, since the preceding text of claims 64 or 71 fail to set forth any reference to "a lipid complex" *per se*.

For these reasons, the claims fail to meet the tenor and express requirements of 35 U.S.C. 112, second paragraph, and are, thus, properly rejected.

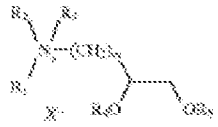
Claim Rejections - 35 USC § 103 (New Grounds of Rejection)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 64, 67, 69-70 and 83-84 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nantz et al. (U.S. Patent No. 5,869,715; Issued 1999, Filed September 1995, already of record) in view of Felgner (WO 91/17424; 1991, already of record).

Nantz et al. teaches cationic lipid compounds that are functional to bind and transport polynucleotides, polypeptides, pharmaceutically substances and other biologically active species through membrane barriers (col.1, l.6-9), wherein the cationic compounds are of the following chemical structure:



, wherein R4 and R5 may each be, *inter alia*, alkyl; m is 1-10; R1 and R3 may each be, *inter alia*, alkyl; X is an anion; and R2 may be, *inter alia*, acyl or acyloxy containing alkyl group (col.3, l.42-67).

The cationic lipid compounds disclosed by Nantz et al. correspond to Applicant's instantly claimed compounds, wherein R1 and R2 are each independently a linear or branched, unsubstituted or substituted C1-C23 alkyl; n is 1-6; R3 and R4 are each independently a linear or branched, unsubstituted or substituted C1-C23 alkyl; m is 1-10; Z is oxygen; and R6 is hydrogen or equivalent to R1, R2, R3 or R4 (i.e., in this case, R6 may be linear or branched, unsubstituted or substituted C1-C23 alkyl).

Nantz et al. fails to explicitly teach the step of combining the disclosed cationic lipid compounds with an anionic molecule to deliver the anionic molecule into a cell (claims 64 and 71).

Felgner teaches that cationic lipid technology using positively charge synthetic cationic lipids in the form of liposomes, or small vesicles, is capable of interacting spontaneously with DNA, which is negatively charged, or anionic, to form lipid-DNA complexes having a net positive charge and are capable of fusing with the negatively charged cell membranes of tissue culture cells to achieve both uptake and expression of the DNA by said cells (p.2, l.28-p.3, l.3). Felgner further teaches that valuable therapeutic agents are most effective in influencing cell function at the subcellular or molecular levels (such as, e.g., natural biological molecules and their analogues or foreign substances, such as drugs) and

are, therefore, preferably incorporated into the cell in order to produce their effect (p.1, l.13-24). Still further, Felgner discloses that intracellular delivery of bioactive agents is particularly useful for, e.g., introducing expressible DNA and mRNA into the cells of a mammal to effect intracellular delivery of beneficial or interesting proteins (p.2, l.1-8).

One of ordinary skill in the art at the time of the invention would have found it *prima facie* obvious to employ the cationic lipid compounds as disclosed by Nantz et al., which are expressly taught to be useful for binding and transporting polynucleotides, polypeptides, pharmaceutically substances and other biologically active species through membrane barriers, in the form of liposomes and combining such liposomes with anionic DNA (i.e., an "anionic molecule" as instantly claimed; see instant claim 64) to form a lipid-DNA complex with a net positive charge to elicit the predictable result of fusing with the negatively charged cell membranes of tissue culture cells to transfect such DNA into the cell such that the cell then expresses the DNA. Such a person would have been clearly motivated to do so in order to predictably effect the intracellular delivery of expressible DNA into cells to produce proteins of interest (e.g., proteins of therapeutic value or proteins of experimental value, etc.).

Conclusion

Rejection of claims 64, 67-74 and 83-87 is proper.

Claims 65-66, 75-82 and 88-90 are **withdrawn** from consideration pursuant to 37 C.F.R. 1.142(b).

No claims of the present application are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leslie A. Royds whose telephone number is (571)-272-6096. The examiner can normally be reached on Monday-Friday (9:00 AM-5:30 PM).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571)-272-0718. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Leslie A. Royds/
Patent Examiner, Art Unit 1614

August 1, 2008

/Ardin Marschel/
Supervisory Patent Examiner, Art Unit 1614